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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,688	01/11/2001	Wolfgang Heil	PLOVIN-2A	7991

23599 7590 05/30/2003

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CHANNAVAJJALA, LAKSHMI SARADA

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1615

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/757,688 Examiner Lakshmi S Channavajjala	HEIL ET AL. Art Unit 1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 January 2003 and 10 March 2003.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 90-96,98-119,122,134 and 138-152 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 90-96,98-119,122,134 and 138-152 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All b) Some \* c) None of:  
1. Certified copies of the priority documents have been received.  
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	6) <input type="checkbox"/> Other: _____

## DETAILED ACTION

Receipt of request for extension of time and amendment F dated 1-2-03; Declaration with attachment and supplemental amendment F dated 3-10-03 are acknowledged.

Claims 90-96, 98-119, 122 and 134 are pending. New claims 138-152 have been added. Accordingly, claims 90-96, 98-119, 122, 134 and 138-152 are remaining in the instant case.

### *Response to Arguments*

Applicant's arguments with respect to claims 90-96, 98-119, 122, 134 have been considered but are moot in view of the new ground(s) of rejection.

### *Claim Rejections - 35 USC § 103*

Claims 90-96, 98-119, 122, 134 and 138-152 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/11680 to Elleisen in view of US Pub. No. 2002/0173487 to Backenfeld et al (hereafter Backenfeld) or Backenfeld in view of Elleisen.

Backenfeld teaches oral pharmaceutical compositions comprising cyclodextrin complexed estrogen and micronized drospirenone for hormone replacement therapy (HRT), female contraception etc (paragraph 0092-0094). Among estrogens, Backenfeld teaches estradiol, particularly ethynodiol (page 3), similar to that claimed. In a preferred embodiment, Backenfeld teaches including micronized drospirenone (DSRP) along with estrogen (page 4, paragraphs 0053-0054 & col. 5, paragraph 006). The amounts of micronized DSRP and estrogen are taught in paragraph 0057, 0058 and Table on page 7 (paragraph 0071). Backenfeld teaches that estrogen and DSRP are to be administered for 21, 22, 2 or 24 consecutive days and placebo for 7, 5, 6, or 4 consecutive days and each day of 7 or less days, a daily dosage unit of estradiol alone (paragraphs 0098-0099). Thus, Backenfeld suggests the

claimed dosage regimens of estradiol + DSRP, cyclical DSRP, estradiol alone and placebo.

Backenfeld teaches cyclodextrin complexed estrogen, whereas instant claims do not recite such a complex. Backenfeld fails to teach the claimed protecting endometrium, deficient estrogen levels, and other symptoms of claim 92. Backenfeld teaches symptoms

'WO teaches hormone replacement therapy (HRT) method comprising administering estrogen and a progestogen for the treatment of pre-menopausal and menopausal symptoms (pages 1, 4, 5). WO teaches both oral and transdermal compositions. The estrogen in the composition comprises estradiol and its esters such as valerate, acetate benzoate, and examples of progestogen include drospirenone (page 15). WO suggests the claimed daily doses of estrogen and drospirenone (DRSP). Although, 'WO does not specifically mention the protection of endometrium by DRSP in their composition, they teach the same composition as claimed, including the claimed daily ranges. Therefore, absent showing evidence on the contrary, the composition of WO possesses the ability to protect endometrium. WO fails to teach micronized drospirenone etc (page 15).

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use a combination of estrogen and micronized DSRP to provide HRT relating to pre-, post- or peri-menopausal related symptoms caused by estrogen deficiency because Elliesen teach that HRT prevents the adverse physiological effects such as hot flushes episodic sweating (page 33) caused during the pre-, post- or peri-menopausal periods. Further, both the references teach dosage regimens the fall within the claimed regimens. Therefore, one of an ordinary skill in the art would have expected to provide relief from the symptoms caused during pre-, post- or peri-menopausal with a combination of estrogen and micronized DSRP.

Double patenting rejection:

Applicants have canceled the composition and kit claims and accordingly, the double patenting rejection over the composition and kit claims has been withdrawn. However, with respect to the double patenting rejection of claims over the co-pending application in view of Elliesen ('349), applicants note that it is only a provisional and the order of issuance of relevant sets of claims should be determined and that when one of the sets are ready for patenting, then the issue will be addressed. Accordingly, the obviousness double patenting rejection has been maintained.

Response to Remarks:

Applicants' remarks and the two Declarations (provided by Dr. Elliesen and Dr. Lipp) were fully considered. In response to the declaration of Dr. Elliesen, examiner has withdrawn the rejection under 35 USC 103(a) as unpatentable over WO 97/11680 in view of Lignieres. However, the arguments regarding the declaration of Dr. Lipp were not found to be persuasive. According to the explanation of Dr. Lipp, isomerization of DSRP to an inactive form occurs in the intestine due to the acidic pH conditions and that applicants showed that micronization hastens the isomerization to an inactive form. Accordingly, applicants state that if providing DSRP in a micronized form could have been expected to increase its surface area and exposure to environment (an argument presented in the last Office Action), such a process would have caused inactivation of the compound. Therefore, applicants conclude that one of ordinary skill in the art would not have been motivated to use micronized form of DSRP. However, the arguments were not found to be persuasive because if it is known that micronized DSRP results

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in an active form, how is it possible that a micronized DSRP in the instant claim is effective in providing HRT and in providing claimed unexpected result of Figure 3 (instant application).

Besides, the newly applied rejection (above) provides a teaching of micronized DSRP.

Accordingly, the declaration of Dr. Lipp and applicants' arguments were not persuasive in light of the new rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 703-308-2438. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Lakshmi S Channavajjala  
Examiner  
Art Unit 1615  
May 29, 2003